Am. J. Trop. Med. Hyg., 92(5), 2015, pp. 1013–1022
doi:10.4269/ajtmh.14-0737

Meteorological Conditions Associated with Increased Incidence of West Nile Virus Disease in the United States, 2004–2012

Micah B. Hahn, Andrew J. Monaghan, Mary H. Hayden, Rebecca J. Eisen, Mark J. Delorey, Nicole P. Lindsey, Roger S. Nasci, and Marc Fischer*

National Center for Atmospheric Research, Boulder, Colorado; Division of Vector-Borne Diseases, Centers for Disease Control and Prevention, Fort Collins, Colorado

Abstract. West Nile virus (WNV) is a leading cause of mosquito-borne disease in the United States. Annual seasonal outbreaks vary in size and location. Predicting where and when higher than normal WNV transmission will occur can help direct limited public health resources. We developed models for the contiguous United States to identify meteorological anomalies associated with above average incidence of WNV neuroinvasive disease from 2004 to 2012. We used county-level WNV data reported to ArboNET and meteorological data from the North American Land Data Assimilation System. As a result of geographic differences in WNV transmission, we divided the United States into East and West, and 10 climate regions. Above average annual temperature was associated with increased likelihood of higher than normal WNV disease incidence, nationally and in most regions. Lower than average annual total precipitation was associated with higher disease incidence in the eastern United States, but the opposite was true in most western regions. Although multiple factors influence WNV transmission, these findings show that anomalies in temperature and precipitation are associated with above average WNV disease incidence. Readily accessible meteorological data may be used to develop predictive models to forecast geographic areas with elevated WNV disease risk before the coming season.

INTRODUCTION

West Nile virus (WNV) is a leading cause of arthropod-borne viral (arboviral) disease in the United States, with over 37,000 reported cases during 1999–2013.[1] An estimated 70–80% of people infected with the virus are asymptomatic; 20–30% develop an acute systemic febrile illness, and < 1% experience neuroinvasive disease (e.g., meningitis, encephalitis, or myelitis).[2–5] WNV was first documented in the United States in New York City in 1999 and subsequently spread westward, reaching the Pacific coast in 2003.[6,7] Since then, WNV has caused seasonal summer outbreaks that vary in size and scope.[7–9] Although some United States regions have reported consistently high incidences of WNV disease, other areas have had only sporadic disease or intermittent outbreaks. No vaccine or specific treatment of WNV is currently available.[10] Reducing mosquito exposure through vector control and personal protective behaviors are the primary forms of prevention.[11] Predicting where and when higher than normal WNV transmission will occur would help direct public health control efforts.

WNV is maintained in an enzootic cycle between mosquitoes and amplifying vertebrate hosts, primarily birds.[12] The virus is transmitted to humans by infected *Culex* mosquitoes. Numerous studies have evaluated the impact of weather on WNV vector or avian host abundance, mosquito infection rate, or incidence of human disease.[6,9–20] However, most of these studies were performed in limited geographic areas or over relatively short time periods. We evaluated the independent effects of temperature and precipitation anomalies on human WNV disease incidence in the United States during 2004–2012. We used national and regional models to assess variation in these relationships in different climatological zones of the United States.

* Address correspondence to Marc Fischer, Arboviral Diseases Branch, Centers for Disease Control and Prevention, 3156 Rampart Road, Fort Collins, CO 80521. E-mail: mfischer@cdc.gov

MATERIALS AND METHODS

Epidemiologic data. WNV disease is a nationally notifiable condition. State health departments report cases to the Centers for Disease Control and Prevention (CDC) through the ArboNET surveillance system.[13] Cases are reported and classified as a neuroinvasive or non-neuroinvasive disease using standard definitions that include clinical and laboratory criteria. Because of the considerable morbidity associated with neuroinvasive disease cases, detection and reporting is assumed to be more consistent and complete than for non-neuroinvasive disease cases. We limited our analysis to WNV neuroinvasive disease cases reported to ArboNET by county for 2004–2012. The WNV disease incidence was calculated using annual population estimates from the U.S. Census Bureau.[14]

For each county and year, we calculated standardized z-scores that described annual WNV disease incidence as the number of standard deviations above or below the mean values in that county for 2004–2012.[15] Using z-scores allowed us to compare counties with substantially different disease incidence and variance on the same scale. Of the 3,109 counties in the continental United States, 1,741 (56%) have never reported a neuroinvasive WNV disease case; as a result, the incidence z-scores are skewed and we modeled increased incidence as a dichotomous variable. We fit models with cutoff z-score values of 0.5, 1.0, 1.5, and 2.0. The magnitude and direction of all effect estimates were similar for all z-scores; therefore, we used a z-score > 0.5 to define above average incidence to increase the sensitivity of the model.

Meteorological data. Monthly mean temperature and total precipitation estimates for 2004–2012 were obtained from the North American Land Data Assimilation System (NLDAS).[16–18] The NLDAS data have a spatial resolution of ~14 × 11 km (0.125°) and were aggregated to the county level by averaging grid cell values for cells inside each county boundary.

In the United States, seasonal WNV disease outbreaks typically peak between June and September. Therefore, meteorological conditions were evaluated from October of the prior

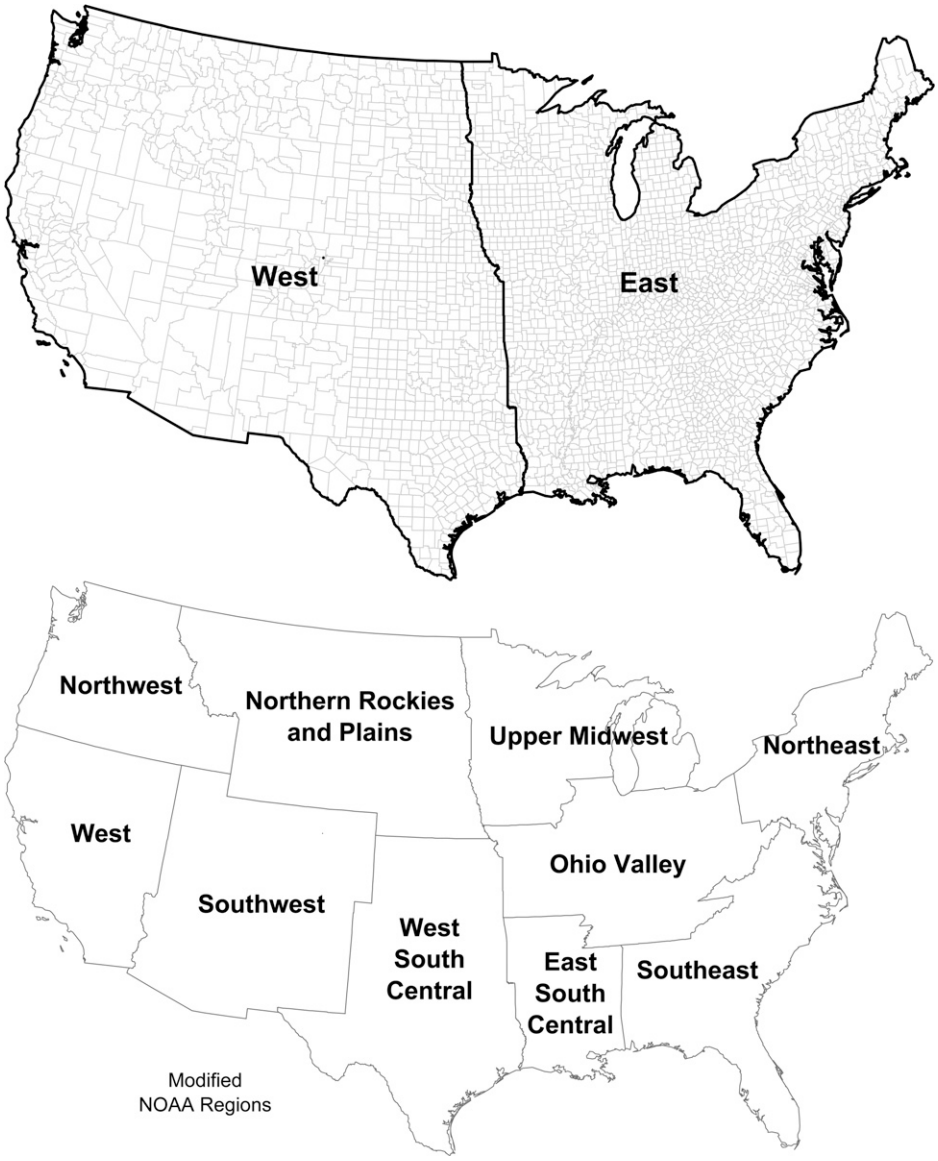

FIGURE 1. Geographic areas used to assess the relationship between temperature and precipitation anomalies and human West Nile neuroinvasive disease.

year through September of the given WNV season. For each county, average annual temperature was calculated by averaging 12 months of temperature data. Average annual total precipitation was calculated for each county by summing the monthly precipitation data. Seasonal meteorological variables were created by averaging monthly temperature and summing precipitation variables for each quarter (i.e., Fall, October–December; Winter, January–March; Spring, April–June; Summer, July–September).

For each county, we calculated standardized z-scores that describe annual and seasonal temperature and precipitation as a number of standard deviations above or below the mean values for 2004–2012. Any non-zero z-score indicates a temperature or precipitation anomaly relative to the average conditions in the county.

United States regions. As a result of geographic differences in climate and WNV transmission, we divided the United States into East and West using state boundaries that run approximately along 95°–100° West longitude (Figure 1). The east-west boundary was chosen because it approximates a climatic divide driven by differences in annual rainfall and the geographic distribution of WNV mosquito vectors and avian reservoirs.[19–21] We further divided the country into 10 climate regions approximately as defined by the National Oceanic and Atmospheric Administration (NOAA).[22] The NOAA regions were chosen because the climate characteristics related to temperature and rainfall within each multistate region are relatively homogeneous. To maintain consistency with the east and west boundary, we divided the NOAA South region into West South Central and East South Central regions along the 95°–100° W longitude line.

National data correlations. To evaluate the independent effects of temperature and precipitation on WNV disease incidence, we modeled the meteorological variables separately. First, we assessed the correlation between z-scores for national WNV disease incidence and average national

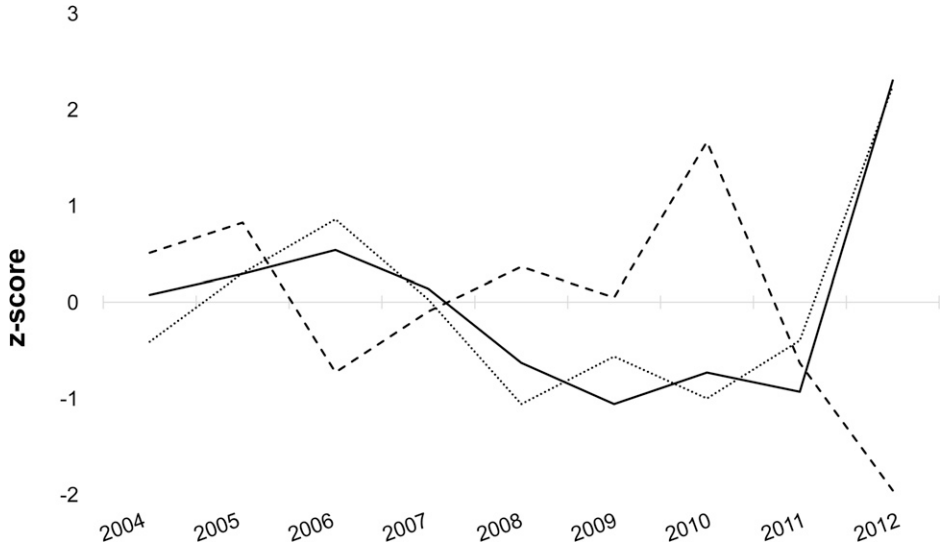

FIGURE 2. Times series from 2004 to 2012 of the annual average temperature (dotted line) and total precipitation (dashed line) z-scores overlaid on the average West Nile virus (WNV) incidence z-score (solid line) relative to the 2004–2012 baseline for the contiguous United States.

temperature for the contiguous United States during 2004–2012. Next, we evaluated the correlation between national disease incidence and total precipitation.

Modeling county-level associations. To evaluate the relationship between WNV disease incidence and meteorological anomalies at a county level, we used generalized estimating equation regression[23] to assess the association between higher than normal WNV disease incidence (modeled as a binary variable) and annual and seasonal temperature and precipitation anomalies for each county in the contiguous United States, the eastern and western United States, and the 10 climate regions. We used an exchangeable working correlation structure, which assumes that the observations within a county are equally correlated over time, based on a comparison of the variance–covariance matrices from exchangeable, autoregressive, and unstructured working correlation structures. For the seasonal temperature and precipitation models, we used a backward stepwise procedure (stay criteria: $P < 0.05$) for variable selection. Results are presented as odds ratios (ORs) with 95% confidence intervals (CIs) that account for multiple comparisons, and statistical tests were performed with an overall Type I error of 0.05. To quantify the increased risk of experiencing above average WNV disease incidence for an absolute change in temperature or precipitation, we calculated the OR for each county given a 1°C increase in temperature or 100 mm more total annual precipitation relative to the 9-year average in that county.

To evaluate the national, east/west, and regional temperature and precipitation models, we used receiver operating characteristic curves to compare the discrimination ability of each model based on the area under the curve (AUC).[24] Using our training data set, we output a continuous predicted probability of experiencing higher than normal WNV incidence for each county for each year from 2004 to 2012. We dichotomized these continuous model predictions using the probability value from the associated receiver operating characteristic curve that simultaneously maximized the sensitivity and specificity so that predicted probability values greater than the cut-off were considered higher than normal WNV years. We compared these dichotomous predictions to the observed dichotomized z-score classification for each county and year to obtain the percent false positives and percent false negatives produced by each model.

RESULTS

National data correlations. National WNV disease incidence z-scores showed a strong positive correlation with average national temperature anomalies during 2004–2012 ($\rho = 0.93$, $P < 0.01$) (Figure 2). The correlation between WNV disease incidence z-scores and national total precipitation anomalies was not significant (Figure 2, $\rho = -0.64$, $P = 0.06$).

County-level models. Almost half of the contiguous U.S. counties (44%) reported above average WNV disease incidence at least one year between 2004–2012 (Figure 3).

Temperature and WNV disease incidence. Higher than normal average annual temperature increased the likelihood that a county experienced higher than normal WNV disease incidence nationally, in the eastern and western United States, and in 7 of 10 NOAA regions (Table 1). This relationship was not significant in the Southwest, West, and Northwest regions. Nationally, for each standard deviation increase in average annual temperature relative to the 9-year average, a county had a 1.7 times (95% CI: 1.6, 1.8) greater odds of experiencing higher than normal WNV disease incidence. Seasonally, winter temperature anomalies were the most consistent predictor of increased disease incidence; above average winter temperatures were associated with higher than normal WNV disease incidence nationally, in the East and West, and in 6 of 10 NOAA regions (Table 2).

The impact of a similar absolute increase in temperature varied by region (Figure 4). On average, counties in the Northeast and Southeast regions had five times the odds (OR = 5.2, 95% CI = 5.0, 5.4) of above average WNV disease incidence for a 1°C increase in temperature above the 9-year average. In the Northern Rockies and Plains region, a 1°C increase in temperature doubled the odds of above average WNV disease incidence (OR = 2.1, 95% CI = 2.0, 2.2),

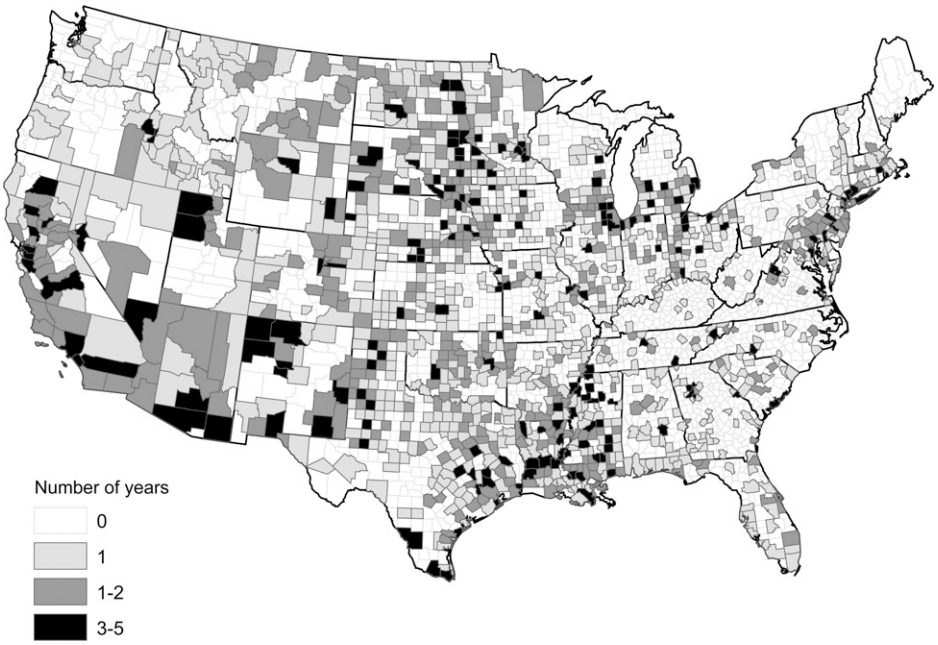

FIGURE 3. Number of years between 2004 and 2012 that a county reported above average incidence of human West Nile virus (WNV), i.e., the annual z-score for human WNV incidence was > 0.5 based on the 2004–2012 average incidence in that county.

although the counties with the highest sensitivity to increases in temperature were clustered in the western portion of the region. Counties in the Upper Midwest, Ohio Valley, and East and West South Central regions had 1.9 times the odds (95% CI = 1.9, 1.9) of above average WNV disease incidence for a 1°C increase in temperature above the 9-year average.

Precipitation and WNV disease incidence. Modeling results showed that for the contiguous United States, lower than normal annual precipitation increased the likelihood that a county would experience higher than average WNV disease incidence that year (Table 1). However, this association only held for four of the five regions in the eastern United States (Northeast, Southeast, Ohio Valley, and Upper Midwest) and for one region in the western United States (Northern Rockies and Plains). By contrast, greater than normal total annual precipitation was associated with increased WNV disease incidence in four of the western regions (West South Central, Southwest, West, and Northwest). This regional variation was also apparent in the seasonal precipitation models (Table 2). Drier than normal fall and spring seasons preceded higher than normal WNV disease incidence seasons in the eastern United States, whereas wetter than normal winters were associated with higher than average WNV disease incidence years in the western United States.

As with temperature, the impact of a similar absolute increase in precipitation varied by region (Figure 4). On average,

TABLE 1

Odds of above average West Nile virus (WNV) incidence in a county for each standard deviation increase in annual average temperature or total precipitation* by region, United States, 2004–2012

Area	Annual temperature z-score			Annual precipitation z-score		
	Odds ratio	95% CI	*P* value	Odds ratio	95% CI	*P* value
National	1.7	(1.6, 1.8)	< 0.01	0.9	(0.9, 0.9)	< 0.01
East/West						
East	1.8	(1.7, 1.9)	< 0.01	0.8	(0.7, 0.8)	< 0.01
West	1.5	(1.4, 1.6)	< 0.01	1.1	(1.0, 1.1)	0.07
Climate region						
Northeast	2.2	(1.9, 2.6)	< 0.01	0.6	(0.5, 0.8)	< 0.01
Southeast	2.2	(1.9, 2.5)	< 0.01	0.7	(0.6, 0.8)	< 0.01
Ohio Valley	1.7	(1.6, 1.9)	< 0.01	0.8	(0.7, 0.8)	< 0.01
Upper Midwest	1.8	(1.6, 2.0)	< 0.01	0.8	(0.7, 0.9)	< 0.01
East South Central	1.7	(1.4, 1.9)	< 0.01	1.0	(0.9, 1.1)	0.82
West South Central	1.4	(1.2, 1.6)	< 0.01	1.3	(1.1, 1.4)	< 0.01
Northern Rockies / Plains	2.1	(1.9, 2.4)	< 0.01	0.6	(0.6, 0.7)	< 0.01
Southwest	1.1	(0.9, 1.3)	0.38	1.4	(1.2, 1.6)	< 0.01
West	1.1	(0.9, 1.3)	0.32	1.5	(1.2, 1.8)	< 0.01
Northwest	1.0	(0.9, 1.2)	0.84	2.0	(1.4, 2.8)	< 0.01

*Climate z-scores are relative to the annual temperature/precipitation from the 2004–2012 baseline period.

TABLE 2

Odds of above average West Nile virus (WNV) incidence in a county for each standard deviation increase in seasonal* temperature or precipitation† by region, United States, 2004–2012‡

	Seasonal temperature z-score											
	Fall			Winter			Spring			Summer		
Area	Odds ratio	95% CI	*P* value	Odds ratio	95% CI	*P* value	Odds ratio	95% CI	*P* value	Odds ratio	95% CI	*P* value
National	1.1	(1.1, 1.2)	< 0.01	1.6	(1.5, 1.7)	< 0.01	1.2	(1.1, 1.2)	< 0.01	–	–	–
East/West												
East	–	–	–	1.8	(1.7, 2.0)	< 0.01	1.1	(1.0, 1.2)	0.01	–	–	–
West	1.2	(1.1, 1.3)	< 0.01	1.3	(1.2, 1.4)	< 0.01	1.2	(1.1, 1.3)	< 0.01	–	–	–
NOAA Region												
Northeast	–	–	–	1.7	(1.4, 2.0)	< 0.01	–	–	–	1.7	(1.3, 2.2)	< 0.01
Southeast	–	–	–	2.1	(1.7, 2.6)	< 0.01	1.5	(1.1, 1.9)	< 0.01	–	–	–
Ohio Valley	–	–	–	1.8	(1.6, 2.0)	< 0.01	–	–	–	–	–	–
Upper Midwest	1.8	(1.4, 2.3)	< 0.01	–	–	–	–	–	–	–	–	–
East South Central	0.8	(0.7, 0.9)	< 0.01	2.9	(2.2, 3.7)	< 0.01	–	–	–	0.8	(0.6, 0.8)	< 0.01
West South Central	0.8	(0.7, 0.9)	< 0.01	2.3	(1.9, 2.9)	< 0.01	–	–	–	0.8	(0.7, 0.9)	< 0.01
Northern Rockies / Plains	2.0	(1.7, 2.4)	< 0.01	–	–	–	1.7	(1.4, 2.1)	< 0.01	–	–	–
Southwest	–	–	–	–	–	–	1.3	(1.0, 1.6)	0.02	–	–	–
West	–	–	–	1.3	(1.0, 1.7)	0.04	–	–	–	–	–	–
Northwest	–	–	–	0.2	(0.1, 0.3)	< 0.01	8.2	(3.0, 22.7)	< 0.01	–	–	–
	Seasonal precipitation z-score											
	Fall			Winter			Spring			Summer		
Area	Odds ratio	95% CI	*P* value	Odds ratio	95% CI	*P* value	Odds ratio	95% CI	*P* value	Odds ratio	95% CI	*P* value
National	0.9	(0.9, 1.0)	0.01	1.2	(1.1, 1.2)	< 0.01	0.8	(0.8, 0.9)	< 0.01	–	–	–
East/ West												
East	0.9	(0.7, 0.8)	< 0.01	–	–	–	0.7	(0.7, 0.8)	< 0.01	–	–	–
West	–	–	–	1.4	(1.3, 1.5)	< 0.01	0.9	(0.9, 1.0)	0.02	–	–	–
NOAA region												
Northeast	–	–	–	0.7	(0.6, 0.9)	< 0.01	0.5	(0.4, 0.6)	< 0.01	–	–	–
Southeast	0.7	(0.5, 0.8)	< 0.01	0.8	(0.7, 0.9)	< 0.01	–	–	–	–	–	–
Ohio Valley	–	–	–	–	–	–	0.6	(0.5, 0.7)	< 0.01	–	–	–
Upper Midwest	0.8	(0.7, 0.9)	< 0.01	1.2	(1.0, 1.3)	0.01	0.9	(0.7, 1.0)	0.04	–	–	–
East South Central	–	–	–	1.3	(1.2, 1.5)	< 0.01	0.8	(0.7, 0.9)	< 0.01	–	–	–
West South Central	–	–	–	1.7	(1.5, 2.0)	< 0.01	0.8	(0.7, 0.9)	< 0.01	–	–	–
Northern Rockies/Plains	0.7	(0.6, 0.8)	< 0.01	–	–	–	0.9	(0.8, 1.0)	0.02	0.7	(0.6, 0.8)	< 0.01
Southwest	1.4	(1.1, 1.7)	< 0.01	1.2	(1.0, 1.5)	0.02	–	–	–	1.2	(1.1, 1.5)	0.01
West	–	–	–	–	–	–	1.5	(1.2, 1.8)	< 0.01	–	–	–
Northwest	1.9	(1.4, 2.6)	< 0.01	2.3	(1.5, 3.3)	< 0.01	–	–	–	1.5	(1.1, 2.0)	0.01

*Fall (Oct–Dec), Winter (Jan–Mar), Spring (Apr–May), Summer (July–Sept).
†Climate z-scores are relative to the temperature/precipitation in a season from the 2004–2012 baseline period.
‡Values selected for each model were based on a backward stepwise procedure with a stay criteria of $P < 0.05$. Variables that were not significant, and therefore dropped from the model, are shown as –.

counties in the Northwest, West, Southwest, and West South Central regions had 1.4 times the odds (95% CI = 1.3, 1.4) of above average WNV disease incidence if they received 100 mm more annual total precipitation than the 9-year average. In contrast, in all other regions (except the East South Central region where precipitation was not significant), the odds of above average WNV disease incidence was lower if they received 100 mm more annual total precipitation than the 9-year average (OR = 0.9, 95% CI = 0.8, 0.9).

Model fit. Based on our AUC values, temperature was more useful than precipitation in discriminating between counties with higher than normal WNV disease incidence and those with normal or below normal incidence in the national (temperature = 0.65 versus precipitation = 0.53), east/west (temperature = 0.67 versus precipitation = 0.59), and regional models (temperature = 0.71 versus precipitation = 0.65) (Table 3). For both temperature and precipitation, the regional models provided better estimates of WNV disease risk than the national or east/west models. The regional temperature model correctly predicted the most counties (61%) and had the lowest percent false positives (37%). There was not substantial variation in the percent false negatives across models.

DISCUSSION

National and regional models showed higher than average temperature in the months preceding a WNV season was associated with increased risk of higher than average WNV disease incidence. Other epidemiologic investigations have found similar associations between warmer than normal temperatures in the months before a WNV season and increased human disease cases using a variety of meteorological measures including fewer cold winter days,[25] warmer mean minimum temperature in January,[26] warmer winter temperatures,[27] and monthly temperature anomalies from the 30-year average.[28] Higher temperature favors greater larval[29] and adult mosquito abundance,[30–33] likely caused by the acceleration of larval emergence, development and adult reproduction, and more successful overwintering of adults or eggs.[34,35] The rate of WNV replication in adult mosquitoes is also positively

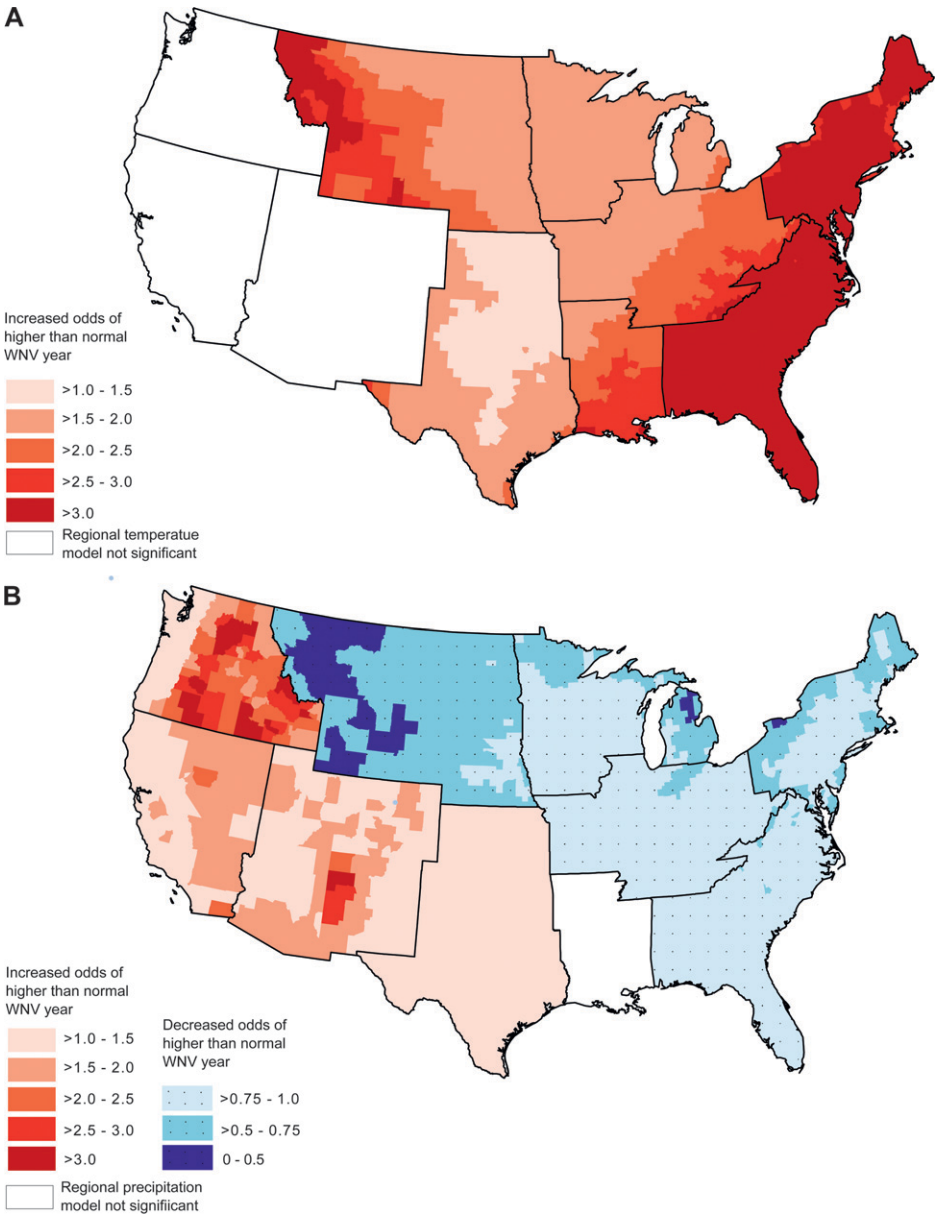

FIGURE 4. Odds of experiencing a higher than normal West Nile virus (WNV) year if the **A**) annual average temperature in a county is 1°C warmer than normal or **B**) the total annual precipitation is 100 mm more than normal.

associated with temperature, which reduces the time interval between a blood meal to when an adult mosquito can transmit the virus to another host[36] and results in an augmented mosquito infection rate.[37] Warmer than normal winter temperatures may also impact bird migration, hatching, or avian community composition,[38,39] all of which have been shown to impact WNV dynamics.[40–43] Finally, higher than normal temperatures during the summer may modify human behavior and influence exposure to infected mosquitoes.

The association between precipitation and WNV disease incidence varied regionally, which may be partly explained by the diversity of WNV disease ecology across the United States. Lower than normal total annual precipitation was associated with increased WNV disease in most eastern regions and the Northern Rockies and Plains, and higher than normal total precipitation was associated with increased WNV incidence in the remaining western regions. The eastern and western United States are climatically distinct, with semi-arid to desert regions dominating the West. In the East, humid continental, temperate, or subtropical regions are present across a latitudinal gradient from north to south. From 2004 to 2012, average annual precipitation in the East was 1,136 mm (SD = 191) compared with 677 mm (SD = 333) in the West. Additionally, the eastern United States is dominated by "urbanized areas" (> 50,000 population) and "urban clusters" (2,500–50,000 population), whereas the western United States has more rural areas.[44] The primary WNV mosquito vectors also vary geographically, with *Culex pipiens* in the northern United States, *Culex quinquefasciatus* in the southern states, and *Culex tarsalis* in the plains and western states with areas that overlap the distribution of the other two vectors.[45] The vectors have different breeding habitat requirements ranging from fresh,

TABLE 3

Area under the curve (AUC) from ROC curves and model evaluation criteria based on the 2004–2012 national training data set, for the annual temperature and precipitation z-score models of above average WNV incidence

Annual climate z-score models	AUC	Classification*		
		Percent correct	Percent false positives	Percent false negatives
National				
Temperature	0.65	54.6	43.0	2.4
Precipitation	0.53	50.4	45.8	3.8
East/West				
Temperature	0.67	53.9	43.9	2.2
Precipitation	0.59	55.5	41.2	3.3
Climate region				
Temperature	0.71	60.6	37.0	2.4
Precipitation	0.65	53.1	44.6	2.3

*Dichotomous predictions for all counties in the contiguous United States for 2004–2012 were compared with the actual dichotomized West Nile virus (WNV) z-scores for each county and year.

sunlit water found in irrigated fields preferred by *Cx. tarsalis*[46] to stagnant, high-nutrient water often in small containers in backyards used by *Cx. pipiens* and *Cx. quinquefasciatus*.[47,48]

As a result of these regional differences in climate, land use, and mosquito distribution and habitat requirements, in the wetter eastern regions of the country where mosquitoes that breed in standing water with high organic content are the dominant WNV vector, less than normal precipitation may create breeding habitats as seasonal streams and ponds begin to dry, leaving behind stagnant pools of water. In urban and suburban areas, catch basins and underground storm drain systems have been implicated as important oviposition and larval development sites.[29] A recent study found that low rainfall favored high larval abundance in these water sources, and a single multi-hour rainfall event exceeding 35 mm was enough to flush almost all larvae from a catch basin.[29] In contrast, in western counties, *Cx. tarsalis* is generally most abundant in rural areas with a high percentage of grasslands, pasture, or irrigated agricultural land.[31,46] In these typically warm and dry regions, excess rainfall may increase WNV risk by creating temporary standing pools of water for female mosquitoes to lay their eggs.[31,33] Bowden and others[49] found that human WNV disease was associated with urban land covers in the Northeast and rural land covers in the western United States, further supporting the suggestion that the contrasting urban, *Cx. pipiens*-driven disease ecology in the eastern United States and the rural, *Cx. tarsalis*-driven ecology in the western United States could account for the variable impact of precipitation on human WNV incidence.

The finding that the relationship between precipitation and WNV disease incidence in the Northern Rockies and Plains region mirrored that of the wetter eastern regions was unexpected given that the average annual total precipitation in this region (564 mm) is more similar to the dry western regions. Unlike the dry but warmer Southwest and West regions, long-term snow accumulation in the Northern Rockies and Plains[19] may ensure sufficient soil moisture in the mosquito breeding season in early spring such that temperature is the limiting environmental condition for mosquito populations. Additionally, the eastern edge of this region, where most of the human WNV cases occur, is environmentally more similar to the Upper Midwest than it is to the western parts of this region, which may explain why the precipitation relationship is similar to the wetter eastern regions. Although the average climate of the Northwest is cooler and wetter than the other western regions, the relationships between temperature, precipitation, and WNV disease were surprisingly similar.

Our results showed that, on average, counties in the eastern United States had a 5-fold increase in the odds of having higher than normal WNV incidence associated with a 1°C higher than normal annual average temperature. For reference, in 2012, the warmest year in the 20th century in the United States,[50] 71% of counties in the contiguous United States experienced an annual temperature at least 1°C higher than the 2004–2012 average. Similarly, we estimated the impact of a 100 mm precipitation anomaly and found significant influences on WNV incidence. In 2012, about 9% of counties in both the East and West received over 100 mm more total annual precipitation than normal.[50]

Our AUC results show that modeling WNV disease incidence regionally provides more accurate estimates of WNV risk than national models, likely caused by geographic differences in climate and mosquito and bird distribution.[19–21] Although the regional models explained more of the variance in human WNV disease incidence than the national or east/west models, a limitation of modeling at the regional scale using political divisions is that there are discrete boundaries between regions that suggest sometimes substantially different relationships between temperature or precipitation anomalies and WNV risk. For example, along the border between Kansas and Missouri, our models suggest that wetter than normal conditions facilitate WNV transmission in Kansas, although the opposite is true in Missouri. In reality, the relationship between precipitation anomalies and WNV transmission is likely more nuanced; however, the number of WNV neuroinvasive disease cases in our data set does not permit modeling in smaller regions. Regardless, the overlap in the distribution of *Cx. tarsalis* with *Cx. pipiens* and *Cx quinquefasciatus* along the east/west boundary could provide a biological basis for the contrasting precipitation impacts across such a limited spatial gradient. In a comparison of precipitation impacts on WNV risk in eastern and western Colorado, Shaman and others[51] speculated that wetter than normal spring seasons in the dry eastern plains may favor *Cx. tarsalis* breeding sites, whereas drier than normal conditions in the wetter mountain west may favor *Cx. pipiens* breeding. In areas where multiple mosquito vectors are present, precipitation anomalies in either direction may provide the ideal breeding sites for one of the vectors.

In addition to temperature and precipitation, many other factors may also influence WNV transmission and disease risk. Among these are seasonal shifts in mosquito feeding preferences from amplifying bird hosts to humans after birds have migrated[42] or differences in land use that impact bird reservoir community composition or viral prevalence.[52–55] Enzootic transmission of the virus can be decreased if mosquitoes feed on low reservoir-competent avian hosts[56] or by herd immunity in the bird population.[57] Others have documented the impact of human behavior and interventions on WNV incidence patterns such as mosquito control, neglected swimming pools that provide mosquito breeding habitat, or having water-holding containers in the backyard.[58–60] Similarly, the use of personal protection such as repellent is influenced by individual risk perception and may vary from year to year depending on media coverage and public health messaging.[61,62]

We have shown that using only annual temperature we can create a model that identifies higher than normal WNV disease incidence in a county with "fair" accuracy.[63] AUC values range from 0 to 1, where 0.5 suggests the model does not discriminate better than random chance, whereas a value of one signifies a perfect test.[64] Our values ranged from 0.53 to 0.71. There are several potential strategies for improving the predictive capability of this model. A univariate modeling approach was used here because our primary objective was to explore the independent associations between temperature or precipitation and WNV incidence and to determine whether proceeding with development of a predictive model for WNV is worthwhile. A multivariate modeling approach that employs seasonal temperature and precipitation variables together, integrates additional meteorological data, and uses non-climatic data such as census information and land cover, will likely explain an even higher percentage of inter-annual variation in WNV disease incidence. Refining the analysis using ecologically or climate-based regions that may more accurately reflect mosquito and bird distributions rather than political borders may also improve the predictive model. Our seasonal model results show that meteorological variables that precede the WNV season are stronger predictors of human WNV incidence than summer temperature and precipitation. Wimberly and others[28] similarly found that December and January temperature anomalies were the most geographically consistent predictor of interannual WNV incidence. This suggests that forecasts of WNV risk based on winter and spring meteorological variables could be made several months in advance of the summer peak of WNV cases, and would not be substantially improved by waiting for summer meteorological variables to become available.

In summary, we have shown that annual temperature and precipitation anomalies are associated with increased WNV incidence. Modeling WNV regionally provides more accurate predictions of WNV risk than a national approach. This study provides a unique regional comparison of the relationships between temperature, precipitation, and WNV anomalies, and our results show that there is variation in the meteorological influences on WNV incidence between different climatological regions of the United States. This study suggests that it may be possible to develop a predictive model that forecasts the likelihood of increased WNV disease incidence in the weeks or months before the onset of the peak transmission season.

Received November 30, 2014. Accepted for publication February 8, 2015.

Published online March 23, 2015.

Acknowledgments: We thank Jennifer Lehman for her assistance obtaining the ArboNET data.

Financial support: This work was funded by the Climate and Health Program of the National Center for Environmental Health, U.S. Centers for Disease Control and Prevention. The National Center for Atmospheric Research is sponsored by the National Science Foundation.

Authors' addresses: Micah B. Hahn, National Center for Atmospheric Research (NCAR), Boulder, CO, and Division of Vector-Borne Diseases, Centers for Disease Control and Prevention, Fort Collins, CO, E-mails: mhahn@ucar.edu or mhahn@cdc.gov. Andrew J. Monaghan and Mary H. Hayden, National Center for Atmospheric Research (NCAR), Boulder, CO, E-mails: monaghan@ucar.edu and mhayden@ucar.edu. Rebecca J. Eisen, Mark J. Delorey, Nicole P. Lindsey, Roger S. Nasci, and Marc Fischer, Division of Vector-Borne Diseases, Centers for Disease Control and Prevention, Fort Collins, CO, E-mails: rjeisen@cdc.gov, mdelorey@cdc.gov, nplindsey@cdc.gov, rnasci@cdc.gov, and mfischer@cdc.gov.

REFERENCES

1. Centers for Disease Control and Prevention, 2013. *West Nile Virus Statistics and Maps*. Available at: http://www.cdc.gov/westnile/statsMaps/. Accessed April 3, 2014.
2. Mostashari F, Bunning ML, Kitsutani PT, Singer DA, Nash D, Cooper MJ, Katz N, Liljebjelke KA, Biggerstaff BJ, Fine AD, Layton MC, Mullin SM, Johnson AJ, Martin DA, Hayes EB, Campbell GL, 2001. Epidemic West Nile encephalitis, New York, 1999: results of a household-based seroepidemiological survey. *Lancet 358:* 261–264.
3. Busch MP, Wright DJ, Custer B, Tobler LH, Stramer SL, Kleinman SH, Prince HE, Bianco C, Foster G, Petersen LR, Nemo G, Glynn SA, 2006. West Nile virus infections projected from blood donor screening data, 2003. *Emerg Infect Dis 12:* 395–402.
4. Zou S, Foster GA, Dodd RY, Petersen LR, Stramer SL, 2010. West Nile fever characteristics among viremic persons Identified through blood donor screening. *J Infect Dis 202:* 1354–1361.
5. Carson PJ, Borchardt SM, Custer B, Prince HE, Dunn-williams J, Winkelman V, Tobler L, Biggerstaff BJ, Lanciotti R, Petersen LR, Busch MP, 2012. Neuroinvasive disease and West Nile virus infection, North Dakota, USA, 1999–2008. *Emerg Infect Dis 18:* 684–686.
6. Nash D, Mostashari F, Fine A, Miller J, O'Leary D, Murray K, Huang A, Rosenberg A, Greenberg A, Sherman M, Wong S, Layton M, 2001. The outbreak of West Nile virus infection in the New York City area in 1999. *N Engl J Med 344:* 1807–1814.
7. Lindsey NP, Staples JE, Lehman J, Fischer M, 2010. Surveillance for human West Nile Virus disease—United States, 1999–2008. *MMWR Surveill Summ 59:* 1–17.
8. Centers for Disease Control and Prevention, 2013. West Nile virus and other arboviral diseases—United States, 2012. *MMWR Morb Mortal Wkly Rep 62:* 513–517.
9. Lindsey NP, Staples JE, Delorey MJ, Fischer M, 2014. Lack of evidence of increased West Nile virus disease severity in the United States in 2012. *Am J Trop Med Hyg 90:* 163–168.
10. Beasley DWC, 2011. Vaccines and immunotherapeutics for the prevention and treatment of infections with West Nile virus. *Immunotherapy 3:* 269–285.
11. Petersen LR, Brault AC, Nasci RS, 2013. West Nile virus: review of the literature. *JAMA 310:* 308–315.
12. Komar N, 2003. West Nile virus: epidemiology and ecology in North America. *Adv Virus Res 61:* 185–234.
13. Centers for Disease Control and Prevention, 2014. *ArboNET Database*. Available at: http://www.cdc.gov/westnile/resourcepages/survResources.html. Accessed May 6, 2014.
14. U.S. Census Bureau, 2014. *U.S. Census Population Estimates*. Available at: http://www.census.gov/popest/. Accessed May 6, 2014.
15. Abdi H, 2007. Z-scores. Salkind N, ed. *Encyclopedia of Measurement and Statistics*. Thousand Oaks, CA: Sage.
16. Xia Y, Mitchell K, Ek M, Sheffield J, Cosgrove B, Wood E, Luo L, Alonge C, Wei H, Meng J, Livneh B, Lettenmaier D, Koren V, Duan Q, Mo K, Fan Y, Mocko D, 2012. Continental-scale water and energy flux analysis and validation for the North American Land Data Assimilation System project phase 2 (NLDAS-2): 1. Intercomparison and application of model products. *J Geophys Res 117:* D03109.
17. Cosgrove B, Lohmann D, Mitchell K, Houser P, Wood E, Schaake J, Robock A, Marshall C, Sheffield J, Duan Q, Luo L, Higgins R, Pinker R, Tarpley J, Meng J, 2003. Real-time and retrospective forcing in the North American Land Data Assimilation System (NLDAS) project. *J Geophys Res 108:* 8842.
18. Mitchell KE, Lohmann D, Houser PR, Wood EF, Schaake JC, Robock A, Cosgrove BA, Sheffield J, Duan Q, Luo L, Higgins RW, Pinker RT, Tarpley JD, Lettenmaier DP, Marshall CH, Entin JK, Pan M, Shi W, Koren V, Meng J, Ramsay BH, Bailey AA, 2004. The multi-institution North American Land Data Assimilation System (NLDAS): Utilizing multiple GCIP

products and partners in a continental distributed hydrological modeling system. *J Geophys Res 109:* D07S90.
19. Cunfer G, 2005. *On the Great Plains: Agriculture and Environment*. College Station, TX: Texas A&M University Press, 304.
20. Reisen W, 1993. The western encephalitis mosquito, *Culex tarsalis*. *Wing Beats 4:* 16.
21. Faanes C, Lingle G, 1995. Biogeographic distribution of breeding birds. *Breed. Birds Platte River Valley Nebraska*. Available at: http://www.npwrc.usgs.gov/resource/birds/platte/distrib.htm. Accessed August 1, 2014.
22. National Oceanic and Atmospheric Administration, 2014. *NOAA Climate Regions*. Available at: http://www.ncdc.noaa.gov/monitoring-references/maps/us-climate-regions.php. Accessed May 12, 2014.
23. Twisk JW, 2003. *Applied Longitudinal Data Analysis for Epidemiology: A Practical Guide*. Cambridge, UK: Cambridge University Press, 57–75.
24. Fielding A, Bell J, 1997. A review of methods for the assessment of prediction errors in conservation presence/absence models. *Environ Conserv 24:* 38–49.
25. Chung WM, Buseman CM, Joyner SN, Hughes SM, Fomby TB, Luby JP, Haley RW, 2013. The 2012 West Nile encephalitis epidemic in Dallas, Texas. *JAMA 310:* 297–307.
26. Manore CA, Davis J, Christofferson RC, Wesson D, Hyman JM, Christopher N, 2014. Towards an early warning system for forecasting human West Nile virus incidence. *PLoS Curr 6.*
27. Winters AM, Eisen RJ, Lozano-fuentes S, Moore CG, Creek C, South D, 2009. Predictive spatial models for risk of West Nile virus exposure in eastern and western Colorado. *Am J Trop Med Hyg 79:* 581–590.
28. Wimberly MC, Lamsal A, Giacomo P, Chuang T, 2014. Regional variation of climatic influences on West Nile virus outbreaks in the United States. *Am J Trop Med Hyg 91:* 677–684.
29. Gardner AM, Hamer GL, Hines AM, Christina M, Walker ED, Ruiz MO, Newman CM, 2012. Weather variability affects abundance of larval *Culex* (Diptera: Culicidae) in storm water catch basins in suburban Chicago. *J Med Entomol 49:* 270–276.
30. Chuang T, Knepper RG, Stanuszek WW, Edward D, Wilson ML, 2011. Temporal and spatial patterns of West Nile virus transmission in Saginaw County, Michigan, 2003–2006. *J Med Entomol 48:* 1047–1056.
31. Chuang T, Hildreth MB, Vanroekel DL, Wimberly MC, 2011. Weather and land cover influences on mosquito populations in Sioux Falls, South Dakota. *J Med Entomol 48:* 669–679.
32. Pecoraro HL, Day HL, Reineke R, Stevens N, Withey JC, John M, Meschke JS, Marzluff JM, 2007. Climatic and landscape correlates for potential West Nile virus mosquito vectors in the Seattle region. *J Vector Ecol 32:* 22–28.
33. Reisen WK, Cayan D, Tyree M, Barker CM, Eldridge B, Dettinger M, 2008. Impact of climate variation on mosquito abundance in California. *J Vector Ecol 33:* 89–98.
34. Nasci RS, Savage HM, White DJ, Miller JR, Cropp BC, Godsey MS, Kerst AJ, Bennett P, Gottfried K, Lanciotti RS, 2001. West Nile virus in overwintering *Culex* mosquitoes, New York City, 2000. *Emerg Infect Dis 7:* 742–744.
35. Hawley W, Pumpuni C, Brady R, Craig G, 1989. Overwintering survival of *Aedes albopictus* (Diptera: Culicidae) eggs in Indiana. *J Med Entomol 26:* 122–129.
36. Reisen WK, Fang Y, Martinez VM, 2006. Effects of temperature on the transmission of West Nile virus by *Culex tarsalis* (Diptera: Culicidae). *J Med Entomol 43:* 309–317.
37. Ruiz MO, Chaves LF, Hamer GL, Sun T, Brown WM, Walker ED, Haramis L, Goldberg TL, Kitron UD, 2010. Local impact of temperature and precipitation on West Nile virus infection in *Culex* species mosquitoes in northeast Illinois, USA. *Parasit Vectors 3:* 1–16.
38. Both C, Bouwhuis S, Lessells CM, Visser ME, 2006. Climate change and population declines in a long-distance migratory bird. *Nature 441:* 81–83.
39. Marra PP, Francis CM, Mulvihill RS, Moore FR, 2005. The influence of climate on the timing and rate of spring bird migration. *Oecologia 142:* 307–315.
40. Hamer GL, Walker ED, Brawn JD, Loss SR, Ruiz MO, Goldberg TL, Schotthoefer AM, Brown WM, Wheeler E, Kitron UD, 2008. Rapid amplification of West Nile virus: the role of hatch-year birds. *Vector Borne Zoonotic Dis 8:* 57–67.
41. Kilpatrick M, Daszak P, Jones MJ, Marra PP, Kramer LD, 2006. Host heterogeneity dominates West Nile virus transmission. *Proc R Soc B Biol Sci 273:* 2327–2333.
42. Kilpatrick AM, Kramer LD, Jones MJ, Marra PP, Daszak P, 2006. West Nile virus epidemics in North America are driven by shifts in mosquito feeding behavior. *PLoS Biol 4:* 606–610.
43. Swaddle JP, Calos SE, 2008. Increased avian diversity is associated with lower incidence of human West Nile infection: observation of the dilution effect. *PLoS ONE 3:* e2488.
44. U.S. Census Bureau, 2010. *Census Urban and Rural Classification and Urban Area Criteria*. Available at: https://www.census.gov/geo/maps-data/maps/pdfs/thematic/2010ua/UA2010_UAs_and_UCs_Map.pdf. Accessed June 18, 2014.
45. Darsie R, Ward R, 2005. *Identification and Geographical Distribution of the Mosquitoes of North America, North of Mexico*. Gainesville, FL: University Press of Florida.
46. Eisen L, Barker CM, Moore CG, Pape WJ, Winters AM, Cheronis N, 2010. Irrigated agriculture is an important risk factor for West Nile virus disease in the hyperendemic Larimer-Boulder-Weld area of North Central Colorado. *J Med Entomol 47:* 939–951.
47. Reiskind MH, Wilson ML, 2004. *Culex restuans* (Diptera: Culicidae) oviposition behavior determined by larval habitat quality and quantity in southeastern Michigan. *J Med Entomol 41:* 179–186.
48. Weinstein P, Laird M, Browne G, 1997. *Exotic and Endemic Mosquitoes in New Zealand as Potential Arbovirus Vectors*. Wellington: Ministry of Health.
49. Bowden SE, Magori K, Drake JM, 2011. Regional differences in the association between land cover and West Nile virus disease incidence in humans in the United States. *Am J Trop Med Hyg 84:* 234–238.
50. NOAA National Climatic Data Center, 2012. *State of the Climate: National Overview for Annual 2012*. Available at: http://www.ncdc.noaa.gov/sotc/national/2012/13. Accessed September 16, 2014.
51. Shaman J, Day JF, Komar N, 2010. Hydrologic conditions describe West Nile virus risk in Colorado. *Int J Environ Res Public Health 7:* 494–508.
52. Ezenwa VO, Milheim LE, Coffey MF, Godsey MS, King RJ, Guptill SC, 2007. Land cover variation and West Nile virus prevalence: patterns, processes, and implications for disease control. *Vector Borne Zoonotic Dis 7:* 173–180.
53. Bradley CA, Gibbs SE, Altizer S, 2013. Urban land use predicts West Nile virus exposure in songbirds. *Ecol Appl 18:* 1083–1092.
54. Brown HE, Childs JE, Diuk-Wasser MA, Fish D, 2008. Ecological factors associated with West Nile virus transmission, northeastern United States. *Emerg Infect Dis 14:* 1539–1545.
55. Chuang T-W, Wimberly MC, 2012. Remote sensing of climatic anomalies and West Nile virus incidence in the northern Great Plains of the United States. *PLoS ONE 7:* e46882.
56. Keesing F, Belden LK, Daszak P, Dobson A, Harvell CD, Holt RD, Hudson P, Jolles A, Jones KE, Mitchell CE, Myers SS, Bogich T, Ostfeld RS, 2010. Impacts of biodiversity on the emergence and transmission of infectious diseases. *Nature 468:* 647–652.
57. Diuk-wasser MA, Molaei G, Simpson JE, Keefe CMF, Armstrong PM, Andreadis TG, 2010. Avian communal roosts as amplification foci for West Nile virus in urban areas in northeastern United States. *Am J Trop Med Hyg 82:* 337–343.
58. Gibney KB, Colborn J, Baty S, Bunko Patterson AM, Sylvester T, Briggs G, Stewart T, Levy C, Komatsu K, MacMillan K, Delorey MJ, Mutebi J-P, Fischer M, Staples JE, 2012. Modifiable risk factors for West Nile virus infection during an outbreak—Arizona, 2010. *Am J Trop Med Hyg 86:* 895–901.
59. Ruiz MO, Tedesco C, McTighe TJ, Austin C, Kitron U, 2004. Environmental and social determinants of human risk during a West Nile virus outbreak in the greater Chicago area, 2002. *Int J Health Geogr 3:* 8.
60. Reisen WK, Takahashi RM, Carroll BD, Quiring R, 2008. Delinquent mortgages, neglected swimming pools, and West Nile virus, California. *Emerg Infect Dis 14:* 1747–1749.

61. Aquino M, Fyfe M, Macdougall L, Remple V, 2004. West Nile virus in British Columbia. *Emerg Infect Dis 10:* 1499–1501.
62. Elliott S, Loeb M, Harrington D, Eyles J, 2008. Heeding the message? Determinants of risk behaviors for West Nile virus. *Can J Public Health 99:* 137–141.
63. Araujo M, Pearson R, Thuiller W, Erhard M, 2005. Validation of species–climate impact models under climate change. *Glob Change Biol 11:* 1–10.
64. Guisan A, Graham CH, Elith J, Huettmann F, 2007. Sensitivity of predictive species distribution models to change in grain size. *Divers Distrib 13:* 332–340.